

Claims 1-25. (Canceled)

Chemical structure of a substituted pyrrolidine derivative (Formula 1). The structure features a pyrrolidine ring with a nitrogen atom (N) substituted with a carbonyl group (C=O) and a quaternary ammonium group (NR₄R₅). The ring is further substituted with R₂, R₇, R₆, R₉, and R₈. A side chain is attached to the ring, consisting of a carbonyl group (C=O) and a nitrogen atom (N) substituted with R₁₀ and R₁.

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R1 represents the side chain of an amino acid or an amino acid derivative, preferably of hydrophobic nature, an alkyl, alkenyl, or alkynyl group having from 1 to 10 carbon atoms, including CH₂CH₃ and CH₂CF₃ ;

R2, identical or different, represents a hydrogen atom, an alkyl group having from 1 to 10 carbon atoms, a hydroxyl function, an alkoxy group, or an (C2-14)aryloxy group, -R2 may also represent a carbonyl group (=O) ;

R3, identical or different, represents the side chain of an amino acid or an amino acid derivative, preferably of hydrophobic nature, an alkyl, alkenyl, or alkynyl group having from 1 to 10 carbon atoms, or a, substituted or not, (C2-14)aryl or (C2-14)aralkyl group, the aryl moiety thereof being optionally interrupted by at least one heteroatom ;

R4 represents a hydrogen atom, an alkyl, alkenyl, or alkynyl group having from 1 to 10 carbon atoms ;

R5 represents a protecting group for the amine function ;

R6 and R7 are the same or different and each represents a hydrogen atom or an, linear, branched, or cyclic, alkyl, alkenyl, or alkynyl group having from 1 to 10 carbon atoms or a, substituted or not, (C2-14)aryl or (C2-14)aralkyl group, the aryl moiety thereof being optionally interrupted with at least one heteroatom ;

R8 and R9 are the same or different and each represents a hydrogen atom or an, linear, branched, or cyclic, alkyl, alkenyl, or alkynyl group having from 1 to 10 carbon atoms or a, substituted or not, (C2-14)aryl or (C2-14)aralkyl group, the aryl moiety thereof being optionally interrupted with at least one heteroatom ;

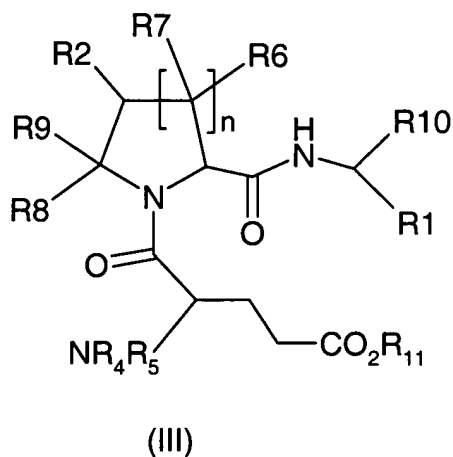
R10 represents an aldehyde (-CHO), an acid group (-COOH), a sulfonic acid (-SO₂OH), -COCOOH group, a radical selected in the group consisting of : -COR, -

COOR, -CONRR', -COCOOR, -SO₂NRR' (a sulfonamide group), -CONHCOR, -COCONRR', -CONHSO₂R, -CHOHCOR, -CHOHCOOR, -CHOHCON-RR', R and R', identical or different, represent an hydrogen atom, a hydroxyl radical, a linear, branched or cyclic alkyl, alkene or alkyne group having from 1 to 10 carbon atoms, an alkoxy group, an amine group or a, substituted or not, (C₂-14)aryl, (C₂-14)aralkyl, or (C₂-14)aralkoxy group, the aryl moiety thereof being optionally interrupted with at least one heteroatom ;

n is 1 or 2 ;

their tautomers, optical and geometrical isomers, racemates, salts, hydrates and mixtures thereof.

27. (New) A compound according to claim 26, wherein the compound corresponds to the following general formula (III) :

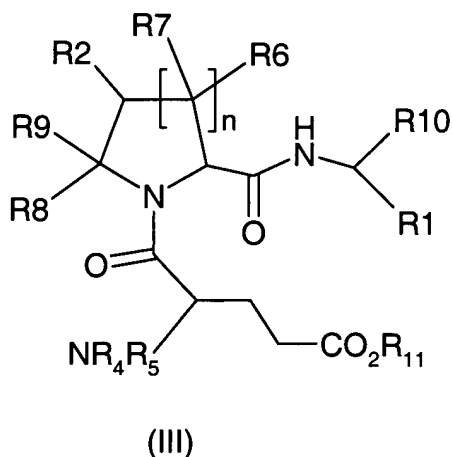


wherein :

R1, R2, R4, R5, R6, R7, R8, R9, R10 and n are as defined above and R11 represents a hydrogen atom, an alkyl group having from 1 to 10 carbon atoms inclusive or a carboxy protecting group ;

their tautomers, optical and geometrical isomers, racemates, salts, hydrates and mixtures thereof.

28. (New) A compound according to claim 26, wherein the compound corresponds to the following general formula (III) :



in which:

R1 represents an alkyl group having from 1 to 10 carbon atoms inclusive or the side chain of an amino acid or an amino acid derivative, including CH₂-CH₃ and CH₂CF₃;

R2 represents a hydroxyl group, an alkoxy group having from 1 to 10 carbon atoms, or -R2 may also represent a carbonyl group (=O) ;

R4 represents a hydrogen atom ;

R5 represents an amine protecting group ;

R6 and R7 are the same or different and each represents a hydrogen atom, a linear or branched alkyl group having from 1 to 10 carbon atoms or a cycloalkyl group having from 1 to 10 carbon atoms, including a cyclohexyl derivative ;

R8 and R9 are the same or different and each represents a hydrogen atom or a linear or branched alkyl group having from 1 to 10 carbon atoms inclusive ;

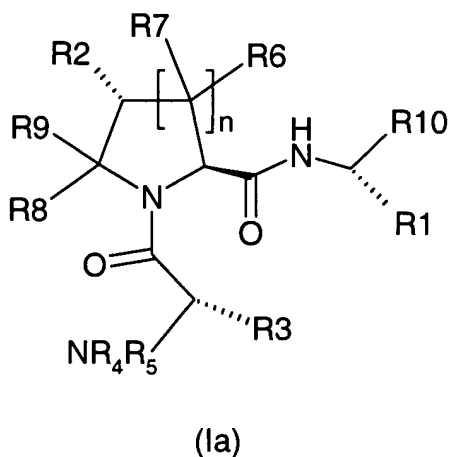
R10 represents an acid group, an ester group, an alkanoyl group, a keto-acid, a keto-ester, a keto-amide or a α -hydroxy-keto derivative ;

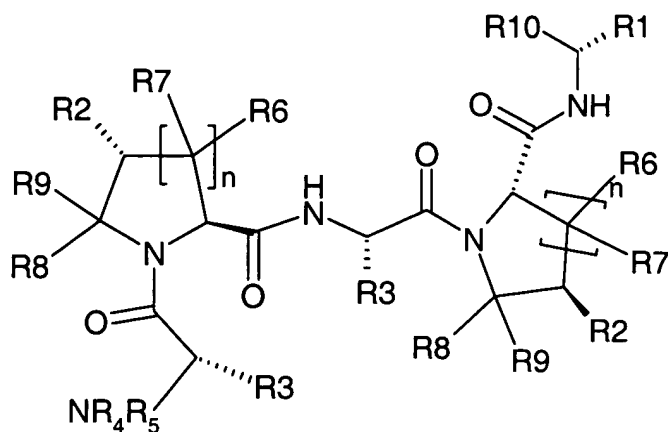
R11 represents a hydrogen atom, an alkyl group having from 1 to 10 carbon atoms inclusive or a carboxy protecting group ; and

n is 1 or 2 ;

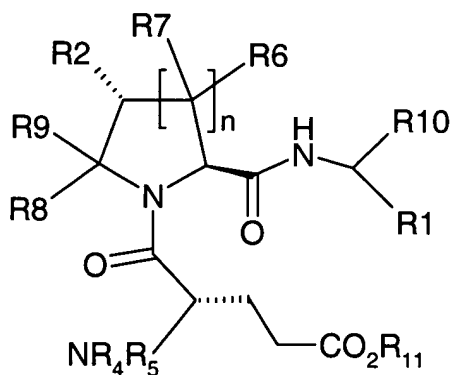
their tautomers, optical and geometrical isomers, racemates, salts, hydrates and mixtures thereof.

29. (New) A compound according to claim 26, wherein the compound has the following formulae (Ia), (IIa) or (IIIa) :





(IIa)



(IIIa)

wherein R1, R2, R4, R5, R6, R7, R8, R9, R10 and n are as defined in claim 1
 and R11 represents a hydrogen atom, an alkyl group having from 1 to 10 carbon atoms
 inclusive or a carboxy protecting group.

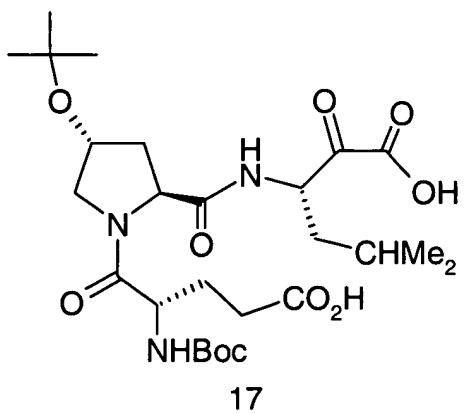
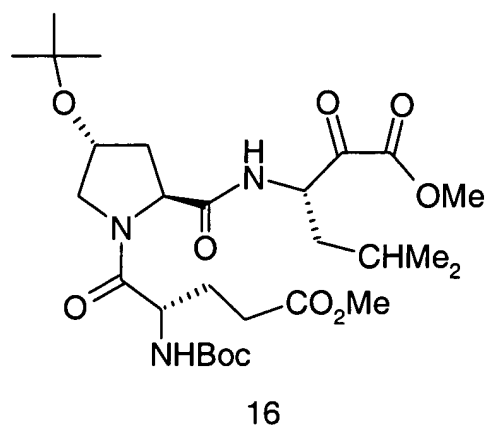
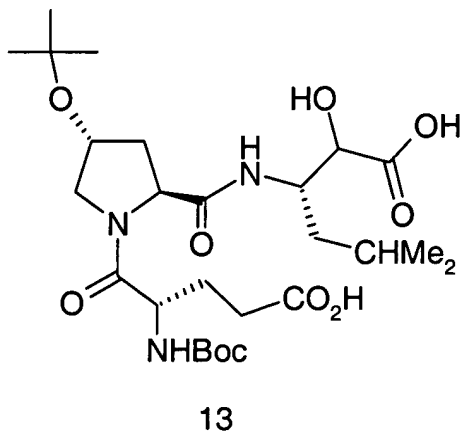
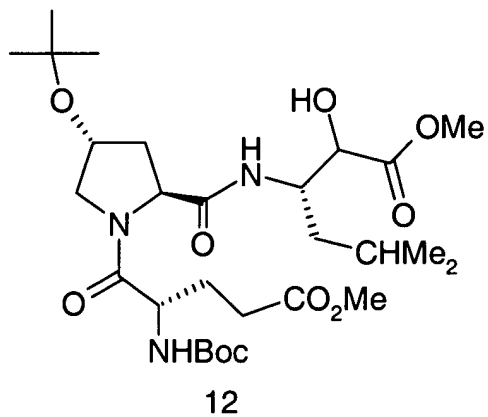
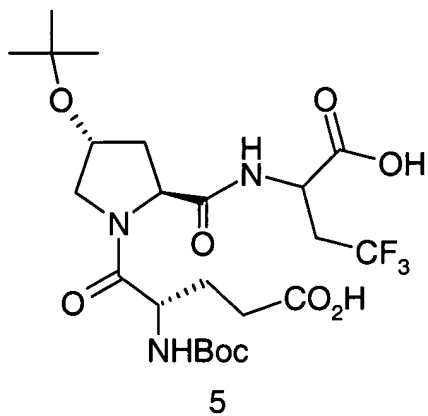
30. (New) A compound according to claim 26, wherein the amino acid side chain
 corresponds to any side chain of the naturally occurring (L form) or synthesized (L or D

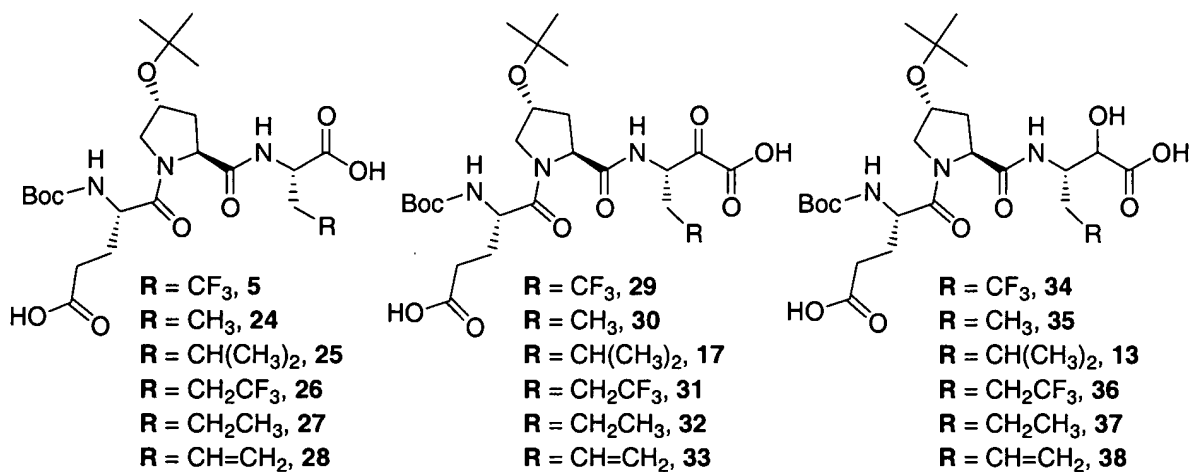
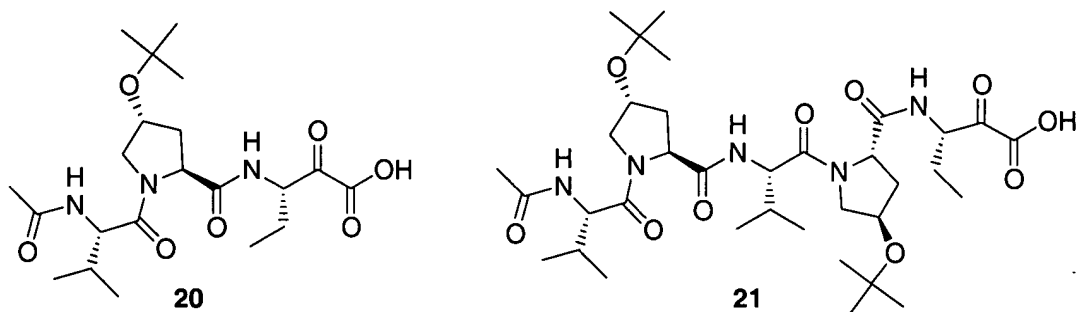
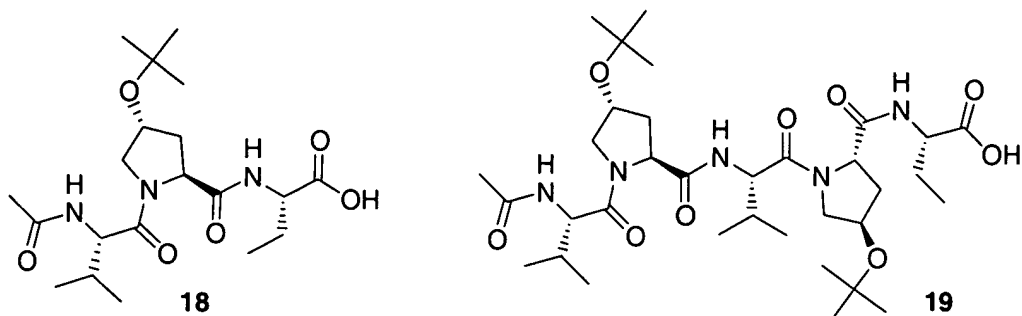
form) aminoacids (in particular alpha-aminoacids and aminocyclopropanoic acid), or derivative thereof, optionally substituted.

31. (New) A compound according to claim 26, wherein the amino acid side chain is selected in the group consisting of $-\text{CH}_3$, $-\text{CH}(\text{CH}_3)_2$, $-\text{CH}_2\text{-CH}(\text{CH}_3)_2$, $-\text{CH}(\text{CH}_3)\text{C}_2\text{H}_5$, H, $-\text{CH}_2\text{OH}$, $-\text{CH}_2\text{CH}_3$, $-\text{CH}(\text{OH})\text{CH}_3$, $-\text{CH}_2\text{SH}$, $-\text{CH}_2\text{CF}_3$, $-(\text{CH}_2)_2\text{-S-CH}_3$, $-\text{CH}_2\text{CH}_2\text{CF}_3$, $-\text{CH}_3\text{C}_2\text{H}_5$, $-\text{CH}_2\text{C}_6\text{H}_5$, $-\text{CH}_2\text{-C}_6\text{H}_4(\text{OH})$, $-\text{CH}_2\text{CONH}_2$, $-(\text{CH}_2)_2\text{CONH}_2$, $-\text{CH}_2\text{COOH}$, $-(\text{CH}_2)_2\text{COOH}$, $-(\text{CH}_2)_4\text{NH}_2$, $-(\text{CH}_2)_3\text{NHC}(\text{NH}_2)_2$, $-\text{CH}_2\text{CH=CH}$ and C_6H_5 .

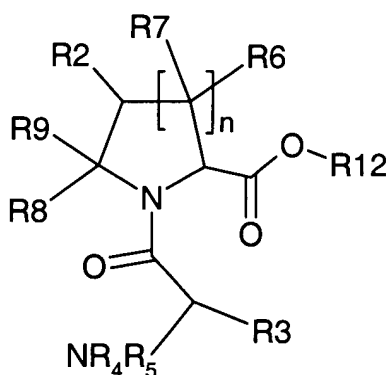
32. (New) A compound according to claim 26, wherein R5 stands for acetyl, benzyloxycarbonyl (Cbz) or t-butyloxycarbonyl (Boc) groups ; and/or R1 stands for $-\text{CH}_2\text{-CH}_3$, $-\text{CH}_2\text{-CF}_3$, $-\text{CH}_2\text{-CH}_2\text{-CF}_3$, $-\text{CH}_2\text{CHCH}_2$ or $-\text{CH}_2\text{-CHMe}_2$; and/or R2 stands for t-butyloxy ; and/or R3 stands for $-(\text{CH}_2)_2\text{COOH}$, $-\text{CH}(\text{CH}_3)_2$, or $-(\text{CH}_2)_2\text{COOCH}_3$; and/or R10 is acid, $-\text{CHOHCOR}$, with R is OH or an alkoxy group (preferably methoxy or ethoxy), keto-acid, keto-ester (preferably $-\text{COCOOME}$, $-\text{COCOOEt}$ or COCOObn), keto-amide (preferably COCONHMe , COCONHEt or COCONHBn) ; and/or R4 is H ; and/or R6 is H ; and/or R7 is H ; and/or R8 is H ; and/or R9 is H; and/or R10 is H and/or $n = 1$.

33. (New) A compound according to claim 26, which is selected in the group consisting of :





34. (New) A compound corresponding to the following formula (V) :

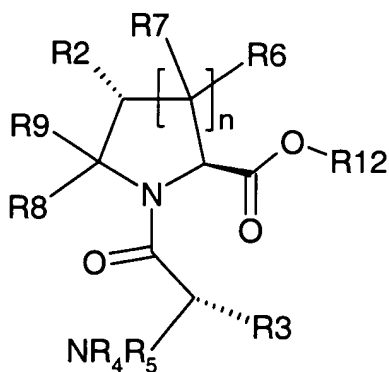


(V)

wherein R2, R3, R4, R5, R6, R7, R8, and R9 are as defined in claim 26 and R12 represents a hydrogen atom, an alkyl group (in particular, methyl, ethyl or t-butyl), alkenyl (allyl), an aralkyl (for instance, benzyl) or a cycloalkyl group; and n is 1 or 2;

their tautomers, optical and geometrical isomers, racemates, salts, hydrates and mixtures thereof.

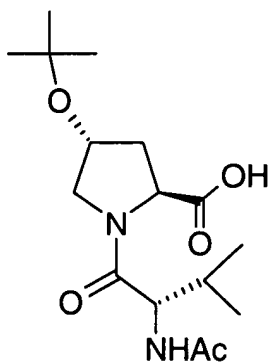
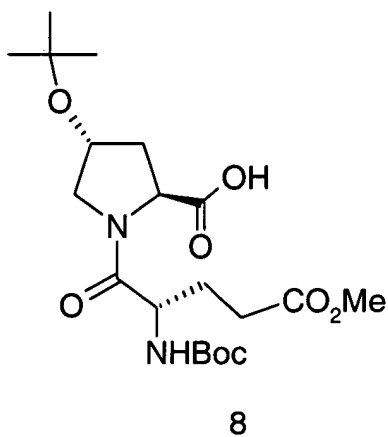
35. (New) A compound according to claim 34, wherein it presents the following formula (Va) :



(Va)

36. (New) A compound according to claim 34, wherein it corresponds to compounds of formula (V) wherein R6, R7, R8 and R9, independently from each other, represents a hydrogen atom, an alkyl, an alkoxy group, or a cycloalkyl group, and preferably a hydrogen atom.

37. (New) A compound according to claim 34, which is selected in the group consisting of:



38. (New) A compound according to claim 34, useful as an active pharmaceutical ingredient, such as an antiviral agent (antiviral HCV agent).

39. (New) A pharmaceutical composition comprising at least one compound as defined in claim 26 and a pharmaceutically acceptable vehicle or support.

40. (New) A pharmaceutical composition according to claim 39, said composition further comprising at least one immunomodulatory agent, other antiviral agent, other inhibitor of hepatitic C protease; inhibitor of other targets in the HCV life cycle, or combinations thereof.

41. (New) A pharmaceutical composition according to claim 39, for treating a disease related to an infection by a virus (preferably flavivirus, such as dengue virus, yellow fever virus, West Nile fever virus, or HCV), bacteria or pathogen dependent upon a serine protease for proliferation

42. (New) A pharmaceutical composition according to claim 39, for treating HCV infection and the like.

43. (New) A pharmaceutical composition according to claim 39, for treating hepatitis C virus infection and complications thereof, in particular chronic hepatitis, cirrhosis or hepatocellular carcinoma and extrahepatic manifestation.

44. (New) A method for the treatment of a disease associated with an infection by a virus (preferably flavivirus, such as dengue virus, yellow fever virus, West Nile fever virus or HCV), bacteria or pathogen dependent upon a serine protease for proliferation, by administering to subject in need of such treatment an effective amount of at least one compound as defined in claim 26.

45. (New) A method for the treatment of a disease associated with HCV infection, by administering to subject in need of such treatment an effective amount of at least one compound as defined in claim 26.

46. (New) A method of evaluating the modulation properties of test compounds towards NS3 serine protease, particularly HCV NS3 serine protease, said method implementing *in vitro* primary cultures of human hepatocytes and compounds as defined in claims 26.

47. (New) A method for screening and/or characterizing compounds that present antiviral activity, in particular antiviral HCV activity, by implementing *in vitro* primary cultures of human hepatocytes and compounds as defined in claim 26.

48. (New) A method for screening and/or characterizing compounds that present antiviral activity, said method comprising the following steps:

a) contacting a test compound with the *in vitro* primary cultures of human hepatocytes described herein in presence of HCV or active part thereof, and

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b) determining the antiviral activity of the test compound in comparison with the antiviral activity of one of the compounds as defined in claim 26.

49. (New) A method to treat or prevent viral contamination of materials by implementing at least one compound as defined in claim 26.